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TOWNSEND and TOWNSEND and CREW LLP

By: /TerrieJ. Rau/

PATENT
Attorney Docket No. 080306-000100US
Client Ref. No. P16809

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Ralph Mocikat

Application No.: 10/716,580

Filed: November 18, 2003

For: EXPRESSION OF IMMUNOGLOBULIN-CYTOKINE FUSION PROTEINS IN MALIGNANT B CELLS

Customer No.: 20350

Confirmation No. 6256

Examiner: WOODWARD, Cherie Michelle

Technology Center/Art Unit: 1647

APPELLANT'S SUPPLEMENTAL REPLY BRIEF UNDER 37 C.F.R. §41.43(b)

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Supplemental Reply Brief is filed pursuant to 37 C.F.R. §41.43(b), in response to the Supplemental Examiner's Answer mailed February 24, 2010.

I. The Question of "Homologous" in the Written Description Rejection

In the Supplemental Examiner's Answer, the Examiner has maintained the rejection of claims 1-5, 7-9, and 11-17 under 35 U.S.C. §112, first paragraph, for alleged inadequate written description. The claimed subject matter is a recombination vector for expressing immunoglobulin-cytokine fusion proteins in malignant B cells. The vector comprises these operably linked components: (a) a continuous region of at least 1.5 kb that is homologous to an at least 1.5 kb segment of the μ intron or the κ intron; (b) at least one DNA sequence encoding a constant region of an immunoglobulin or a part of the constant region; (c) a DNA sequence encoding a cytokine; and (d) a marker gene that is selectable in eukaryotic B cells and contains a functional enhancer region.

In the Reply Brief of February 3, 2010, Appellant points out that the Examiner's Answer unfairly presents arguments for the written description rejection on new grounds never discussed before. The Examiner's particular argument is that, because the claimed vector comprises a continuous region of at least 1.5 kb that is homologous to an at least 1.5 kb segment of the μ intron or the κ intron, a "skilled artisan would not be apprised that Appellant was in possession of a generic homologous region of a genus of κ introns without knowing something more about the structure of the homologous region required for the vector." In the Supplemental Examiner's Answer, the Examiner argues that the written description rejection in the Examiner's Answer contains no new grounds and that the same rejection was made in the Office Action of October 18, 2007, as well as in the Final Office Action of April 3, 2008. Furthermore, the Examiner argues that "[t]he issue of 'homology' to an at least 1.5 kb segment is and has remained a critical central issue throughout the prosecution of the instant application not only in the written description rejection, but also in the other rejections of record." See pages 3-4 of the Supplemental Examiner's Answer.

Appellant respectfully disagrees with the Examiner. While the written description rejection has been made in the previously Office Actions, the focus of the

discussion is consistently on the question whether adequate description is provided for the various components of the claimed recombination vector, and not on the scope afforded by the "homologous" language. For example, on page 11 of the Office Action mailed March 5, 2007, the Examiner states,

> In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is a genera of vectors encoding generic cytokine-immunoglobulin fusion proteins; a genera of vectors encoding a genera of immunoglobulins; a genera of vectors comprising DNA encoding a cytokine; a genera of vectors encoding a genera of marker genes; a genera of vectors encoding a genera of enhancers; a genera of vectors encoding a genera of nucleic acids homologous to a region of comprising the Cμ or Cκ enhancer; a genera of vectors encoding a genera of bacterially compatible regulatory units; a genera of vectors encoding a genera of domains from a human immunoglobulin chain; a genera of vectors encoding a genera of non-species specific chimeric immunoglobulins; a genera of vectors encoding a genera of interleukins; a genera of vectors encoding a genera of interferons; a genera of vectors encoding a genera of colony-stimulating factors; a genera of vectors encoding a genera of lymphokines; or a genera of vectors encoding a genera of growth factors. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the claimed generas.

This very same language is entirely repeated on page 4 of the Office Action mailed October 18, 2007, and again on pages 4-5 of the Office Action mailed April 3, 2008, and then once more on page of the Final Office Action mailed January 6, 2009.

It is therefore clear that throughout the prosecution history the Examiner has consistently taken the position that the written description requirement is not met because the specification does not provide a sufficient number of representative species for each genus: vectors encoding cytokine-immunoglobulin fusion proteins;

immunoglobulins; cytokines; marker genes; enhancers; nucleic acids homologous to an at least 1.5 kb segment of the μ intron or the κ intron; bacterially compatible regulatory units; human immunoglobulin chains; interleukins; interferons; colony-stimulating factors; lymphokines; and growth factors. No distinction has even been made between the variants within the meaning of a polynucleotide sequence "homologous" to an at least 1.5 kb segment of the μ or κ intron and the species within the genus of polynucleotide sequences encoding immunoglobulins, cytokines, marker genes, enhancers, *etc.* While there should be no doubt from the state of the pertinent art that species within the genus of immunoglobulins, cytokines, marker genes, enhancers, *etc.* are known and therefore in possession of any person of ordinary skill in the art, the question of possession with regard to the "homologous" sequence variants is an entirely different one and would require consideration of a different set of factors. This question was not raised until the Examiner's Answer. Appellant therefore contends that it would be unfair to permit the Examiner, at the appeal stage, to rely on this newly raised, never before discussed point to support the written description rejection.

With regard to the anticipation and obviousness rejections, where the Examiner argues in the Supplemental Examiner's Answer that the issue of "homology" remains a focal point of the arguments on both sides, Appellant again respectfully disagrees and contends that the central issue of the anticipation and obviousness rejections is not and has never been this sequence "homology"; rather, the central issue is the interpretation of the word "continuous." More detailed discussions in the next section will further illustrate this point.

To reiterate, sustaining the written description rejection is to take the position that a skilled artisan would not believe the present inventor had in his possession the claimed recombination vector, even though the components of the vector were all known in the art at the effective filing date of this application. The question concerning the sequence variants "homologous" to an at least 1.5 kb segment of the μ or κ intron was

not discussed during prosecution and therefore cannot be relied upon at the appeal stage as the basis for the written description rejection. As such, Appellant respectfully requests the reversal of the written description rejection under 35 U.S.C. §112, first paragraph, because the Examiner has failed to provide an adequate or appropriate basis for supporting the rejection.

II. The Question of "Continuous" in the Anticipation/Obviousness Rejections

In the Supplemental Examiner's Answer, the Examiner maintains the rejection of claims 1-5, 7-9, and 11-17 under 35 U.S.C. §103(a) for alleged obviousness over the Polack reference in view of the Mocikat reference and the Mucke reference. The Examiner appears to reiterate her view, by pointing to pages 23-26 of the Examiner's Answer, that "the claims, as written, do not require that the 'homologous' region to 'an at least 1.5 kb segment of the μ intron or the κ intron' to be continuous. Instead, the 'homologous' region may be comprised of a multiplicity of segments so long as they are homologous to the μ intron or the κ intron and when placed in the claimed vector are a total of at least 1.5 kb in length." See the first paragraph on page 24 of the Examiner's Answer.

Appellant cannot agree with the Examiner's interpretation of "continuous," because the interpretation is directly contradictory to the plain English meaning of this word. According to the Merriam-Webster Online Dictionary, "continuous" means "marked by ***uninterrupted extension in space, time, or sequence***." A copy of this entry is provided in Exhibit A. It is therefore clear that anyone reading the language in claim 1, "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the κ intron," would understand that this language describes an uninterrupted or unbroken polynucleotide sequence having a defined minimal length as well as a sequence homology. There is simply objective basis that the Examiner has identified or would be able to identify either in the specification or else where to support

her assertion that "a continuous region" can be reasonably construed as "a multiplicity of segments."

Appellant also disagrees with the Examiner's interpretation of the word "continuous" because her interpretation would render this word completely meaningless as recited in the pending claims. As explained on page 6 of the Reply Brief, to adopt the Examiner's interpretation (*i.e.*, the "homologous" region may be comprised of a multiplicity of segments so long as they are homologous to the μ intron or the κ intron and when placed in the claimed vector are a total of at least 1.5 kb in length), one would then find this limitation met by virtually ***any*** polynucleotide sequence greater than 1.5 kb in length, since the homologous fragments as suggested by the Examiner could be as small as a single nucleotide, which will always find homology in a target sequence.

Moreover, the claim structure unequivocally indicates that components (a), (b), (c), and (d), are operably linked with other in the recombination vector, whereas each of the components is in itself an uninterrupted polynucleotide sequence. This claim structure thus precludes the unreasonable interpretation of "multiplicity of segments" joined together in a vector to form a "continuous region" of component (a), as suggested by the Examiner.

The Examiner's unreasonable interpretation of "continuous" finds support in neither the dictionary meaning of this word nor the specification. This is inconsistent with the established case law. The Federal Circuit has held in *In re Morris*, 44 USPQ2d 1023 (Fed. Cir. 1997) that the PTO is not required, in the course of prosecution, to interpret claims in applications in the same manner as a court would in an infringement law suit. Rather, the "PTO applies to verbiage of the proposed claims the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in applicant's specification." According to the Federal Circuit in *In re Am. Acad. of Sci.*

Tech. Ctr. F3d 1359, 1364 (Fed. Cir. 2004), the PTO should determine the scope of claims not solely based on the claim language but should make the broadest reasonable construction "in light of the specification as it would be interpreted by one of ordinary skill in the art." In the instant case, the Examiner is ignoring the plain English meaning of the word "continuous" and has in essence disregarded the claim limitation of "a continuous region," all without identifying any basis in the specification.

In summary, because the cited references together fail to provide the claim limitation of "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the κ intron" as one of ordinary skill in the art would properly interpret it, Appellant contends that the rejections under 35 U.S.C. §102 and §103 are improper and must be reversed.

III. Conclusion

In view of the foregoing, Appellant respectfully requests that the written description rejection under 35 U.S.C. §112, first paragraph, anticipation rejection under 35 U.S.C. §102(e), and obviousness rejections under 35 U.S.C. §103(a) be reversed.

Respectfully submitted,

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Attachment (Exhibit A)
CG:cg
62590153 v1

EXHIBIT A

continuous

Main Entry: **con·tin·u·ous**
Pronunciation: \kən-'tin-yü-əs\
Function: *adjective*
Etymology: Latin *continuus*, from *continēre* to hold together — more at CONTAIN
Date: 1673
1 : marked by uninterrupted extension in space, time, or sequence
2 *of a function* : having the property that the absolute value of the numerical difference between the value at a given point and the value at any point in a neighborhood of the given point can be made as close to zero as desired by choosing the neighborhood small enough
synonyms see CONTINUAL
— **con·tin·u·ous·ly** *adverb*
— **con·tin·u·ous·ness** *noun*

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"continuous." Merriam-Webster Online Dictionary. 2010. Merriam-Webster Online. 21 April 2010 <http://www.merriam-webster.com/dictionary/continuous>

APA Style
continuous. (2010). In *Merriam-Webster Online Dictionary*. Retrieved April 21, 2010, from http://www.merriam-webster.com/dictionary/continuous